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THIN ENDOMETRIUM. WAYS TO SOLVE THE PROBLEM

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Key words: assisted reproductive technologies, infertility, endometrial thickness, in vitro fertilization, thin endometrium, embryo implantation.
Tayanch so'zlar: yordamchi reproduktiv texnologiyalari, bepushtlik, endometriy qalinligi, in vitro urug'lantirish, "yupqa" endometriy, embrionning implantatsiyasi.
Ключевые слова: вспомогательные репродуктивные технологии, бесплодие, толщина эндометрия, экстракорпоральное оплодотворение, тонкий эндометрий, имплантация эмбриона.

Methods of treatment aimed at increasing the thickness of the endometrium include anti-inflammatory therapy, intensive administration of estrogen and progesterone drugs, drugs that improve uterine blood flow, surgical interventions, physiotherapy procedures. For many years, methods of intrauterine exposure have been developed, which have mainly anti-inflammatory and immunomodulatory properties, therefore they are more acceptable in the practice of pre-preparation of the endometrium.

YUPQA ENDOMETRIY. MUAMMONI HAL QILISH USULLARI

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Toshkent tibbiyot akademiyasi, Toshkent, O'zbekiston

Endometriyning qalinligini oshirishga qaratilgan davolash usullari yallig'lanishga qarshi terapiya, estrogen va progesteron preparatlarini intensiv yuborish, bachadon qon aylanishini yaxshilaydigan dorilar, jarrohlik aralashuvlar, fizioterapiya muolajalarini o'z ichiga oladi. Shu bilan birga, to'plangan materiallarning so'nggi tahlillari endometriyning qalinligi va implantastiyaga tayyor bo'lishi faqatgina yallig'lanishga qarshi va immunomodulyatorlar bilan davolashning yetarli emasligini ko'rsatadi.

ТОНКИЙ ЭНДОМЕТРИЙ. СПОСОБЫ РЕШЕНИЯ ПРОБЛЕМЫ

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Методы лечения, направленные на увеличение толщины эндометрия, включают противовоспалительную терапию, интенсивное введение препаратов эстрогена и прогестерона, препаратов, улучшающих маточный кровоток, хирургические вмешательства, физиотерапевтические процедуры. В течение многих лет разрабатывались методы внутриутробного воздействия, которые обладают в основном противовоспалительными и иммуномодулирующими свойствами, поэтому они более приемлемы в практике предварительной подготовки эндометрия.

According to domestic and foreign authors, the prevalence of infertility reaches 15-18%, in some regions of Uzbekistan — 19%, and the frequency of spontaneous miscarriage in the first trimester of pregnancy remains at the level of 15% [6]. The decrease in female fertility has many reasons, among which the share of the uterine factor of infertility in an isolated or combined variant accounts for 22-59%. It is known that the prevalence of pathological changes in the endometrium in infertility reaches 86%, with ineffective attempts of in vitro fertilization (IVF) — 74.4% [8]. Currently, it has been established that the state of the endometrium plays an important role in the causes of infertility and miscarriage in women. The thickness and maturity of the endometrium are clearly visible during ultrasound with a vaginal sensor. Before implantation, its thickness should be at least 8 mm. It is known that the thinner the endometrium, the less chance of a favorable outcome of pregnancy. Therefore, the term "thin endometrium" exists in modern literature, since it is the most complex and completely unexplored phenomenon in modern reproduction. Sufficient thickness of the endometrium is very important for the normal implantation of the embryo in the uterine cavity. It is important to note that the frequency of pregnancy decreases in patients with low uterine blood flow, which indicates a close relationship between uterine blood supply and endometrial receptivity.

Methods and materials. 40 women aged 25 to 35 years with primary or secondary infertility and the presence of a "thin endometrium" that does not respond to previously performed hormonal stimulation or physiotherapy treatment were examined. The average age of the patients was 27

years. All patients underwent a comprehensive examination, including the collection of anamnestic data, standard clinical and laboratory studies, a study of the hormonal profile on the 2nd-3rd day of the menstrual cycle, ultrasound of the pelvic organs on the 5th-7th day of the menstrual cycle, dopplerometry and Pipel biopsy of the endometrium on the 7th-11th day of the menstrual cycle. The effectiveness was monitored by ultrasound monitoring with measurement of endometrial thickness and blood flow dopplerometry on the 7th, 9th and 12th days of the menstrual cycle. All patients on the 8th day of the menstrual cycle were randomized into 2 groups: with moderate lag in endometrial development - M-echo≥5 mm (n=24) and extreme lag in endometrial development - M-echo<5 mm (n=16). Each of the groups, depending on the therapy received, was divided into two more. Patients of the 1st subgroup (n=14) with moderate lag in endometrial development during treatment with hormone replacement therapy (HRT) were given intrauterine irrigation and submucosal injection of autoplasm containing platelets; the 2nd subgroup (n=10) with moderate lag in endometrial development were patients who received HRT in the form of monotherapy, without stimulation of platelet autoplasm regeneration. The 3rd subgroup (n=8) included patients with extreme lag in endometrial development (M-echo <5 mm), who also underwent intrauterine irrigation and paracervical submucosal injection of autoplasm containing platelets against the background of HRT treatment. Patients of the 4th subgroup (n=8) with extreme lag in endometrial development received only HRT preparations. In the expected fertile cycle, especially when ovarian function is stimulated, the use of HRT (estrogens) in women with a "thin endometrium" is justified. We used transdermal forms of estrogens (Divigel), which have a number of advantages over oral estradiol intake due to high bioavailability and the possibility of easy dose variation. Estradiol preparations can also be prescribed at the stage of preparation for the fertile cycle in cases when the cause of the "thin endometrium" is ovarian insufficiency. The dose was selected individually under the control of ultrasound (the value of the M-echo of the endometrium). Estrogens were prescribed according to a 21-day regimen, during the last 10 days they were combined with progestins (Didrogesterone 10-20 mg / day, micronized progesterone 200 mg/ day). Intrauterine and paracervical administration of autoplasm containing platelets was carried out as a pre-gravidar preparation, against the background of HRT, in the late phase of proliferation (9th or 10th day) of the menstrual cycle once during 3 menstrual cycles. The undoubted advantage of the introduction of autoplasm containing platelets is the increased blood supply to the mucous membrane of the uterine body, as well as the combined anti-inflammatory effect with the improvement of growth functions, which allows treatment in compliance with the principle of "proliferation without inflammation". When examining endometrial biopsies, the following immunohistochemical markers were determined: transforming growth factor (TGF) and vascular endothelial growth factor (VEGF). It is important to recognize not only the long-term, at least 6 months, preservation of the effect of therapy, but also the increase in positive dynamics. This indicates the ability of the autoplasm containing platelets to restore its own regenerative potential of female reproductive organs. Statistical processing of the data obtained to determine the differences in endometrial thickness in the comparison groups was carried out using the Student parameter comparison method. The differences were considered statistically significant at $p<0.05$.

Results. Initial monitoring demonstrated similar endometrial maturation disorders in all patients. A significant ($p<0.05$) increase in endometrial thickness in the proliferative phase of the cycle compared with baseline values was noted after therapy using irrigation of the uterine cavity with autoplasm containing platelets already at the 3rd month of follow-up in the 1st and 3rd subgroups, while HRT alone did not give a significant effect. The positive result was maintained until the 6th month of follow-up in the 3rd subgroup and progressed even more in the 1st. Thus, the effect of autoplasm containing platelets on the endometrium turned out to be more significant compared to therapy that included only HRT preparations. When conducting an immunohistochemical study in patients treated for "thin endometrium" with autoplasm containing platelets in the 1st and 3rd subgroups, an increase in the expression of the most important regeneration regulators TGF - 5.1±0.4 and VEGF - 4.7±0.9 was determined compared with the expression of those in patients of

the 2nd and 4th subgroups, where only HRT was performed, respectively 1.9±0.1, 1.8±0.5 and 1.7±0.1, 1.5±0.5, due to what caused increased blood supply in the uterine mucosa and stimulation of endometrial growth. With dopplerometry, uniform vascularization of the endometrium and sub-endometrial layer was visualized in the 1st and 3rd subgroups, and in the 2nd and 4th subgroups, a decrease in endometrial blood flow and the absence of sub-endometrial blood flow were noted.The frequency of pregnancy was assessed in 20 women with infertility, 12 of them received a course of ovulation stimulation (previous attempts at stimulation were unsuccessful). Pregnancy occurred in 11 (55%) patients: in 7 out of 7 women of the 1st subgroup, in 1 out of 5 patients of the 2nd subgroup, in 3 out of 4 patients of the 3rd subgroup, in the 4th subgroup of women, pregnancy did not occur in anyone. In 4 patients of the 1st subgroup, pregnancy occurred at the 3rd month of treatment, in the remaining patients of this subgroup, pregnancy occurred at the 4th month. In patients of the 3rd subgroup, pregnancy occurred at the 5th month of treatment.Comparison of intergroup differences in the effectiveness of therapy is not possible due to the small number of observations and significant differences in infertility factors in the groups. However, there has been a trend. It is necessary to recognize the high potential of intrauterine irrigation of autoplasm containing platelets as a means of preparing for the restoration of fertility in women with infertility.

Conclusion. The use of procedures for irrigation of the endometrium of the uterine cavity with autoplasm containing platelets and its introduction into the submucosal space paracervically in patients with "thin endometrium" showed that the method has a positive effect, and in most patients there is a significant growth of the endometrium by the end of treatment. The thickness of the endometrium in the examined subgroups was significantly greater than in the comparison subgroups ($p<0.05$). Thus, such therapy can be recommended for use in the practice of an obstetrician -gynecologist when preparing patients for an in vitro fertilization program. The method of treating patients with "thin endometrium" by intrauterine irrigation with autoplasm containing platelets and its paracervical submucosal administration is an effective, minimally invasive, fairly simple and safe method of treatment that does not require complex equipment. Provides patients with a low degree of pain and the absence of complications.

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